

Appl. No.: 10/560,497
Response Dated: July 14, 2008
Reply to Office Action of April 14, 2008

REMARKS/ARGUMENTS

Claims 1-21 are pending in the instant application. The following remarks are believed to be fully responsive to the Office Action.

35 USC § 103 (a) Rejection

Claims 1-21 stand rejected under 35 USC § 103(a) as being unpatentable over U.S. Patent No. 5,948,940 to Malthe-Sorensen et al. (“Malthe-Sorensen”).

On page 3 of the current Office Action, the Examiner states that “the thrust of applicant’s arguments is that Malthe-Sorensen fails to teach or suggest applicant’s 1-methoxy-2-propanol as a reaction solvent and applicants allege that even though the solvent in question only differ by one carbon, they act very differently”. Further, the Examiner states that “applicants argue how the cited reference differs from the instant invention, but the obviousness test under 35 U.S.C. 103 is whether the invention would have been obvious in view of the prior art taken as a whole”.

Applicants respectfully submit that arguments concerning the obviousness of using 1-methoxy-2-propanol have been provided in both responses dated 09/25/2008 and 02/28/2008. However, certain comments made by the Applicants have not been commented by the Examiner. Sections from said responses are repeated in italics below and we respectfully

Appl. No.: 10/560,497

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request the Examiner consider these arguments and state why it still is considered obvious to try 1-methoxy-2-propanol with a reasonable expectation of success.

“...In addition it was known from WO02/083623, as discussed in the present application, page 2, lines 1-2, to use 1-methoxy-2-propanol as solvent in the purification by recrystallization of iohexol”.

“...one skilled in the art would in fact not have a reasonable expectation of success when using 1-methoxy-2-propanol. The fact that a solvent is known for its use as the dominant solvent in the crystallisation step of the same process would clearly teach away from using the same in the alkylation step. ‘Teaching away’ simply means teaching a solution that would not lead to the claimed subject matter. As noted by the Federal Circuit:

A reference may be said to teach away when a person of ordinary skill, upon [examining] the reference would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. (emphasis added).

Para-Ordnance Mfg. v. SGS Importers Int'l, 73 F.3d 1085 (Fed. Cir. 1995).

In the alkylation step of Malthe-Sorensen it is required that the solvent shows good solubility for 5-(acetamido)-N,N'-bis(2,3-dihydroxypropyl)-2,4,6-triiodoisophthalamide and that the product (iohexol) does not precipitate during the reaction, whereas in the purification step the solvent used should show little solubility for the product (iohexol). A

Appl. No.: 10/560,497

Response Dated: July 14, 2008

Reply to Office Action of April 14, 2008

person skilled in the art would therefore not expect that 1-methoxy-2-propanol could be used as the dominant solvent in both the alkylation and the purification step, and would not think or suggest using 1-methoxy-2-propanol as an alternative to 2-methoxy-ethanol in the production described by Malthe-Sorensen".

Further, on page 3 of the Office Action, the Examiner holds that "Malthe-Sorensen clearly suggests to one having ordinary skill in the art the use of similar solvents, so it would have been obvious to use 1-methoxy-2-propanol in the Malthe-Sorensen process with a reasonable expectation of success". Applicants respectfully disagree. Applicants are the assignee of Malthe-Sorensen and if it would have been obvious to use other solvents than 2-methoxy-ethanol those solvents would clearly have been incorporated. In fact, there are no statements in Malthe-Sorensen suggesting the use of other solvents other than 2-methoxy-ethanol simply because Malthe-Sorensen concerns the specific use of 2-methoxy-ethanol and 2-methoxy-ethanol only. The fact that Malthe-Sorensen does not speak in general of solvents, but only of 2-methoxy-ethanol specifically clearly does not imply "suggesting the use of similar solvents", rather to the contrary. If the use of other solvents was considered possible that would clearly have been stated. Applicants respectfully wish to ask the Examiner to share his views on this. Applicants also wish to remind the Examiner that it is impermissible within the framework of 35 U.S.C. §103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443 (Fed. Cir. 1986). (emphasis added). Applicants further note that "the prior art itself must provide a motivation

or reason for the worker in the art, without the benefit of the Applicant's specification, to make necessary changes in the reference device". See, *Ex parte Chicago Rawhide Manufacturing Co.*, 226 U.S.P.Q. 438 (PTO Bd. App. 1984).

Finally, on page 3 of the Office Action, the Examiner holds that "applicants allege that even though the solvent in question only differ by one carbon, they act very differently and attempt to demonstrate so by way of comparative data shown in table 1 and 2. However, results in tables 1 and 2, such as yield/purity of the product and the amount of other impurities, are not significantly different from the closest prior art". Applicants respectfully submit that the data were not introduced to demonstrate that solvents only differ by one carbon can act differently. The data shown in table 1 and 2 were introduced to demonstrate that surprisingly and unexpectedly 1-methoxy-2-propanol could be used as an alternative solvent to 2-methoxy-ethanol showing the same, and even slightly better, purity of iohexol. Even though a slight increase in purity can make a great difference in a large scale production, the initial motivation was to find, if possible, an alternative to 2-methoxy-ethanol used today.

In addition to the arguments discussed above other aspects supported the belief that 1-methoxy-2-propanol could not be used as solvent in the current process, thereby making it unobvious to try. These aspects are also addressed in the attached Declaration from one of the inventors, Ole Magne Homestad. In short, 2-ehoxyethanol was considered as an alternative solvent but was found to have too poor solubility. Knowing that 1-methoxy-2-propanol was even less polar there were no reason to pursue 1-methoxy-2-propanol as

Appl. No.: 10/560,497

Response Dated: July 14, 2008

Reply to Office Action of April 14, 2008

solvent. In addition, one could consider adding co-solvents to improve solubility, but knowing that such addition to 2-methoxy-ethanol used in the current process worsen the selectivity only supported the belief that 1-methoxy-2-propanol could not be used.

To expect one skilled in the art reading Malthe-Sorensen to try 1-methoxy-2-propanol as an alternative solvent would clearly involve using hindsight. The skilled artisan would have to:

1. Think of trying alternative solvents even though Malthe-Sorensen specifically concerns the use of 2-methoxy-ethanol and in no way suggests that other solvents might work.
2. Think of 1-methoxy-2-propanol as an alternative solvent among a vast number of compounds.
3. Disregard the known facts indicating that 1-methoxy-2-propanol would not work as solvent in the alkylation step.

Accordingly, Applicants respectfully request that the Examiner withdrawal the rejections for claims 1-21 under 35 U.S.C. §103(a) and direct that these claims be allowed.

Appl. No.: 10/560,497
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CONCLUSION

Upon entry of this Amendment, claims 1-21 remain pending. Applicants submit that all outstanding issues have been addressed, and that claims 1-21 are in condition for allowance, which action is earnestly solicited.

The Commissioner is hereby authorized to charge any fees under 37 CFR §1.16(j) or 37 CFR 1.136(a) which may be required, or credit any overpayment, to Deposit Account No. 502-665 in the name of GE Healthcare, Inc.

Should any other matters require attention prior to allowance of the application, it is requested that the Examiner contact the undersigned.

Respectfully submitted,

/Craig Bohlken/
Craig Bohlken
Reg. No. 52,628

GE Healthcare, Inc.
101 Carnegie Center
Princeton, NJ 08540
Phone (609) 514-6530
Fax (609) 514-6572
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